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Stochastic Simulation of Human Pulmonary Blood Flow Based on Anatomic and Elasticity Data

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STOCHASTIC SIMULATION OF HUMAN PULMONARY BLOOD FLOW BASED ON ANATOMIC AND ELASTICITY DATA

by

Jun Shi

A Thesis

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Abstract

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In order to fully understand the function of the lungs, it is important to determine the transit time of the pulmonary circulation. However, a practical model to estimate the transit time is difficult to be found in literature, because of the high complexity of the whole pulmonary circulation system. This study developed a computing model of steady blood flow in human lungs based on detailed morphology and elasticity data by Huang et al (1996) [5], which incorporated a Diameter-Defined Strahler System to simulate a human lung branching system.

A stochastic simulation approach was introduced. Considering Huang's connectivity data between different levels as a probability matrix, the stochastic simulation model can simulate the blood flow in the hierarchical structure of a pulmonary circulation system without constructing the whole structure. At the same time, the model calculated the transit time and output blood pressure. The model efficiently produced the transit time frequency distribution of the human arterial and venous trees, which agree with the lung experiments from humans and animals. Such a simulation model has the advantage of the low computing cost and the high flexibility.

Keyword: blood flow, pulmonary circulation, computer model, human lung

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1. Introduction

The research conducted in this thesis focuses on the human lung and more specifically the pulmonary circulation system. The pulmonary circulation begins at the main pulmonary artery receiving venous blood pumped by the right ventricle. The main pulmonary artery then divides into right and left pulmonary arteries, each of which branches successively into lobar arteries. The branching process continues until the pre-capillary arterioles are formed, which are followed by the capillary network. The blood leaving the capillaries drains into the ostcapillary venules. The venules gradually converge into progressively larger veins and finally unite to form the four large veins that lead into the left atrium.

The pulmonary circulation attracted much less attention of research efforts compared to the systemic circulation. It was not until 1958 that the Chicago Heart Association organized the world's first conference dedicated to the lung circulation. Since then there has been an explosion of research activity and remarkable progress has been made in the understanding of the physiological mechanisms of pulmonary circulation in both normal and disease states. Fishman [1] summarized the history of physiological research in pulmonary circulation in the last century. Reeves and Rubin [8] presented a review of advances made in the past 50 years in three aspects of the lung circulation: oxygen regulation, endothelial contribution to vascular tone, and control of composition of the pulmonary arterial wall.

According to the methods of their investigation, mainly two categories of studies are related to the pulmonary circulation: experimental and modeling studies. The experimental approach includes experimental measurements of pressure, flow, vessel topology, and vessel compliance in animals or humans, analyzing the recorded data, developing new techniques and methods for measurements and data analysis, and determining the biological mechanisms hidden behind the data. Modeling studies consider the vascular network as a certain kind of mathematical system and analyze pulmonary circulation by the use of mathematical calculations or computer simulation.

In this thesis, the modeling approach is selected. Particularly the study will present how to model the distribution of the transit time of the pulmonary circulation under certain blood pressure. Chapter 2 lists related research work which is the base for the modeling effort. Chapter 3 describes the detailed mathematical methods implemented. Chapter 4 presents the simulation results which will show the comparison with existing experimental findings.

2. Literature Review

To construct a model to represent the entire pulmonary circulation system, detailed morphometric and mechanical properties of the vessels are needed. The vessels are branched into different orders with a separate set of parameters for each order. The principles of continuum mechanics are employed to derive the pressure-flow relationship in the vessel tubes and the capillary bed. Equations for arteries and veins of all orders as well as equations for the capillary bed are then concatenated in sequence to complete the circulation circuit. Flow and pressure distributions are obtained by solving the equations sequentially.

2.1 Morphometric and elastic property of human lung

Morphometric information of the human pulmonary arteries and veins contains the vessel diameter, the length, and the branching pattern. Based on silicone elastomer casts, Huang [2] constructed a vessel system which consists of 15 orders of arteries between the main pulmonary artery and capillary sheet and 15 orders of veins between the capillary sheet and left atrium. The branching pattern of this system follows that of Kassab et al. [6,7] A diameter-defined Strahler ordering system is defined in which the capillaries are counted as vessels of order 0. The smallest non-capillary vessels are named vessels of order 1. Two order 1 vessels unite to form a larger vessel of order 2, and so on.

Other information for vessels includes apparent viscosity of the blood and compliance, which are collected from different sources. Zhou [10] summarized in her dissertation morphometric and elasticity data of pulmonary veins and arteries as shown in Table 2.1 and 2.2, respectively. Table 2.3 summarizes a set of parameters for capillary sheet used in our computation.

Table 2.1 Morphometric and Elasticity Data of Pulmonary Veins of Man at P_A-P_{pl} = 10 cmH_2O (Data from Huang et al. [5] if not otherwise indicated)

Order	Number of Branches Nn	Diameter D_0n (cm)	Length Ln (cm)	Apparent Viscosity μ (cP)	Compliance β ($10^{-4}Pa^{-1}$)
15	4	1.2970	3.5680	4.0	0.708*
14	8	0.8650	3.4990	4.0	0.708*
13	22	0.5860	1.9490	4.0	0.708*
12	62	0.4000	2.6490	4.0	0.708*
11	126	0.2880	1.7900	4.0	0.708*
10	286	0.1990	1.4780	4.0	0.708*
9	870	0.1420	1.1240	4.0	0.708*
8	2134	0.0900	0.6780	4.0	0.708
7	7442	0.0620	0.4790	4.0	0.887
6	31134	0.0380	0.2920	4.0	1.260
5	146050	0.0230	0.1500	4.0	1.260
4	906102	0.0130	0.1060	4.0	1.798
3	4332666	0.0067	0.0380	3.5	0.433
2	16988490	0.0031	0.0210	3.0	0.625
1	79647106	0.0018	0.0130	2.5	1.010

*: Unknown compliance coefficients obtained by extrapolating to the nearest order of vessels.

Table 2.2 Morphometric and Elasticity Data of Pulmonary arteries of Man at P_A-P_{pl} = 10 cmH_2O (Data from Huang et al. [5] if not otherwise indicated)

Order	Number of Branches Nn	Diameter D_0n (cm)	Length Ln (cm)	Apparent Viscosity μ (cP)	Compliance β ($10^{-4}Pa^{-1}$)
1	102411624	0.0020	0.0220	2.5	0.698
2	28114394	0.0036	0.0260	3.0	0.482
3	10203806	0.0056	0.0360	3.5	0.361
4	4513692	0.0097	0.0450	4.0	0.361*
5	1348338	0.0150	0.0680	4.0	0.361*
6	571544	0.022	0.108	4.0	1.135
7	172040	0.034	0.192	4.0	0.932
8	44008	0.051	0.281	4.0	0.877
9	12450	0.077	0.373	4.0	1.238
10	3448	0.116	0.658	4.0	1.281
11	900	0.175	1.235	4.0	1.281*
12	254	0.271	1.807	4.0	1.281*
13	86	0.416	2.597	4.0	1.281*
14	14	0.734	3.569	4.0	1.281*
15	4	1.480	2.53	4.0	1.281*
16	1	3.0	9.05	4.0	1.281*

*: Unknown compliance coefficients obtained by extrapolating to the nearest order of vessels.

Table 2.3 Morphometry, elasticity and blood viscosity data of the capillary sheet

Symbol	Value
h_0	3.5 μm
α	0.127 $\mu m/cmH_2O$
$\bar{L}$	1188 μm
S	0.88
A	126 m^2
μ	1.92 cP
K	12
F	1.8

2.2 Pressure-flow relation in steady flow condition

For pulmonary circulation, pressure-flow relations are studied in two conditions: steady flow and pulsatile flow. In steady flow condition, oscillations in blood flow are neglected and mean pressure and flow are concerned. Changes in the relations between mean pressure and mean flow reflect the function of the lung vascular system and are important indicators of certain disorders. For example, patients with mitral stenosis usually have increased left atrial pressure and passive pulmonary arterial hypertension.

The study in steady flow condition, which is mainly addressed in this thesis, is the base for the future study in pulsatile flow condition.

Pressure-flow relation of arteries and veins in steady flow condition

It was shown that for pulmonary arteries and veins, the vessel diameter D changes linearly with the appropriate transmural pressure ΔP,

$$\frac{D}{D_0} = 1 + \beta \Delta P \tag{2.1}$$

Here D_0 is the tube diameter when transmural pressure is zero and β is the compliance coefficient of the vessel wall defined by Yen et al. [10]. Then for a viscous incompressible fluid in vessel tube, the steady flow is governed by Poiseulle's law and can be presented as

$$\frac{640 \mu\beta D_0 L}{\pi}\dot{Q} = D_0^5\left[(1 + \beta\Delta P_{entry})^5 - (1 + \beta\Delta P_{exit})^5\right] \tag{2.2}$$

where μ is the apparent viscosity of blood, L is the length of the vessel, $\dot{Q}$ is the flow rate in the vessel, ΔP_{entry} and ΔP_{exit} are transmural pressures at the entry and exit ends of the vessel. This is called the fifth power law.

When applying the fifth power law in computation, ΔP is calculated as follows 10. For pulmonary vessels with diameters much larger than the alveolar diameter,

$$\Delta P = P - P_{pl} \tag{2.3}$$

Whereas for vessels with diameters smaller than the alveolar diameter,

$$\Delta P = P - P_A \tag{2.4}$$

Here, P is blood pressure, P_A is airway pressure and P_{pl} is pleural pressure.

Pressure-flow relation of capillary sheet in steady flow condition

According to the sheet flow theory [2], the dense network of capillary blood vessels in pulmonary alveolar wall is modeled as a sheet of fluid flowing between two membranes held apart by a large number of regularly spaced posts. If the local blood pressure is larger then the alveolar gas pressure, then the sheet thickness can be derived as

$$h = h_0 + \alpha\left(P - P_A\right) \tag{2.5}$$

Where h is the sheet thickness, h_0 is the thickness of capillary sheet at zero pressure difference when the pressure decreases from positive values, α is the compliance constant of the capillary sheet, P is blood pressure and P_A is airway pressure.

Based on Eq. (2.5), the pressure-flow relationship in capillary sheet is derived as [4]

$$\dot{Q} = const\left(h_a{}^4 - h_v{}^4\right) = const\left\{\left[h_0 + \alpha\left(P_{art} - P_A\right)\right]^4 - \left[h_0 + \alpha\left(P_{ven} - P_A\right)\right]^4\right\} \tag{2.6}$$

Here $\dot{Q}$ is the volume flow rate, h_a is the sheet thickness at the arteriole end, h_v is the sheet thickness at the venule end, and P_{art} and P_{ven} are pressures at the corresponding arteriole and venule. The constant $const$ equals to

$$\frac{SA}{4\,\mu\,kf\,\overline{L}^2\,\alpha} \tag{2.7}$$

Where A is alveolar area, S is the vascular-space-tissue ratio, representing the fraction of the blood volume over a sum of the volumes of the vascular space and the posts. μ is the apparent viscosity of blood in the capillary sheet. k and f are dimensionless factors which describe alveolar structural geometry. $\overline{L}$ is the average length of streamlines between an arteriole and a venule.

Equations (2.5) and (2.6) are valid only when $P_{ven} \geq P_A$. If $P_{ven} < P_A$, it is said to be in zone 2 condition and “waterfall” occurs. The sluicing gate is located at the junction of the capillary sheet and its draining venule. Hence in zone 2 condition h_v tends to 0, and the flow depends only on h_a.

In our calculation, losses due to turbulence and bifurcation are ignored. A repeated application of Eq. (2.2) to each order of arteries and veins as well as the application of Eq. (2.6) to the capillary sheet make a complete pulmonary circulation system.

2.3 Transit time distribution in human lungs

A pulmonary circulation system can be considered as a distributed network of vessels of various lengths and diameters [11]. An important way to analyze such a network is to characterize the transit time distribution. Transit time is defined as the length of time it takes for a red blood cell to travel through the lung. Different cells take different paths in traveling. Transit times vary from streamline to streamline. In analogy to the statistical distribution of a random variable, the transit time distribution of a given lung is defined as a frequency function of the transit time, denoted as f(t), for which f(t)dt is equal to the fraction of the fluid that enters the lung whose transit time lies between t and t+dt [2]. The distribution of pulmonary transit time reflects perfused vascular volume and contact time between blood and vascular surface area, both of which affect gas exchange and metabolic functions of the pulmonary endothelium.

As described by Fung [2] the transit time, depends obviously on the path a blood cell takes in the lungs. Since different cells take different paths the transit times are not constant. The distribution is given by the sheet flow theory which allows for the following transit theoretical transit time calculations to be developed [6].

$$f(t) = \frac{1}{20}\delta(\tau - 1) + 1.678e^{-2(\tau-1)} + \frac{1}{45}e^{-0.2(\tau-1)} \tag{2.8}$$

Using this calculation the theoretical transit time distributions in the pulmonary arteries, capillaries, and veins were calculated by Fung [4].

Experimentally, different methods have been used to study pulmonary transit time distribution and they all use the same basic mechanism: some tracer particles are introduced into the blood and their activities recorded over time [12,13,14]. These experimental results provided benchmarking points for simulation methods at certain given blood pressure condition.

In previous years, research on pulmonary circulation calculation and simulation has been executed. McLaurine [9] pointed out the importance of determining transit time distribution of the pulmonary circulation to fully understand the function of the lungs. In the dissertation, the frequency distributions of the arterial and venous trees and the capillary sheet were convoluted together to obtain the total transit time for the pulmonary circulation. All biological conditions and parameters were considered as dependent statically distributed variables which can be used to generate the frequency distribution of the arterial and venous trees.

On the other hand, Zhou [12] constructed a complex arterial network model close to the real arterial system in terms of size and topology. Gravity flow algorithm was used to solve the network flow problem, which produces the maximum flow in a flow network with segments of different sizes, accompanied with the method of back propagation training. By applying these sophisticated computer algorithms, the transit time distributions were calculated.

The idea of statistical sampling was introduced in McLaurine's dissertation, which gave an indication of a new approach for this problem. However, the significant benefits of statistical sampling faded by trying to construct the whole pulmonary tree before calculation. As a result, as both researchers put it, the scale of pulmonary circulation system was too big for even some super computing systems. The method proposed in this thesis benefits from both research efforts and resolves this issue in the scale of the whole circulation system without increasing the computing load.

3. Methodologies

In a simulating perspective, a pulmonary circulation includes the arterial tree where the blood flows from top to bottom, the pulmonary sheet which is similar to a traffic network, and the venous tree where the blood flows from bottom to top. Assume there is an independent blood particle traveling through the whole network. At each of the crossroads, the blood cell will determine which vessel to traverse. The probability of taking a certain next level road will be determined by some probability matrix. In between two crosses, the blood cell will travel the tube or tunnel which is constrained by the flow mechanism. If the blood cell travels enough times in the system, we can measure the transit time distribution statically viewpoint.

3.1 Probability matrixes

Huang's study also provided two connectivity matrixes, which define the branching pattern of human pulmonary arteries and veins, respectively. The connectivity matrix of pulmonary arteries is shown in Table 3.1. The connectivity matrix of pulmonary veins is shown in Table 3.2. Both are two-dimensional matrices. MaxOrder is the maximal order for the arterial tree and the venous tree, i.e., 15X15. Details about the numbers in these two tables are available in Huang et al. [5].

Table 3.1 Connectivity matrix of the arterial tree (Data from Huang et al. [5])

```
double ConnectMatrix[MaxOrder][MaxOrder] = {
        {0.17,2.54,1.11,0.38,0.02,0.01,0.02,0,0.02,0,0,0,0,0,0},
        {0,0.23,1.67,0.97,0.17,0.09,0.06,0.04,0.02,0,0,0,0,0,0},
        {0,0,0.26,1.44,0.63,0.28,0.2,0.19,0.11,0.03,0,0,0,0,0},
        {0,0,0,0.18,1.96,1.5,0.93,1.07,0.65,0.16,0.03,0,0,0,0},
        {0,0,0,0,0.06,1.81,1.1,0.81,0.83,0.45,0.12,0.02,0,0,0},
        {0,0,0,0,0,0.12,2.54,1.16,0.83,0.93,0.71,0.2,0.05,0,0},
        {0,0,0,0,0,0,0.25,2.52,1.08,1.08,1.49,0.94,0.43,0,0},
        {0,0,0,0,0,0,0,0.28,2.06,1.26,1.63,1.45,0.43,0,0},
        {0,0,0,0,0,0,0,0,0.21,2.38,1.47,0.88,0.81,0.33,0},
        {0,0,0,0,0,0,0,0,0,0.21,2.52,1.35,1.48,0,0},
        {0,0,0,0,0,0,0,0,0,0,0.25,2.43,0.95,0.33,0},
        {0,0,0,0,0,0,0,0,0,0,0,0.14,2.57,1,0.5},
        {0,0,0,0,0,0,0,0,0,0,0,0,0.37,3.5,1.5},
        {0,0,0,0,0,0,0,0,0,0,0,0,0,0,3.5},
        {0,0,0,0,0,0,0,0,0,0,0,0,0,0,0.5}
};
```

Table 3.2 Connectivity matrix of the venous tree (Data from Huang et al. [5])

```
double ConnectMatrix[MaxOrder][MaxOrder] = {
    {0.38,2.59,1.24,0.01,0,0,0,0,0,0,0,0,0,0,0},
    {0,0.53,1.8,0.2,0.03,0.01,0,0,0,0,0,0,0,0,0},
    {0,0,0.28,3.23,1.13,0.82,0.42,0.06,0.02,0,0,0,0,0,0},
    {0,0,0,0.4,3.16,2.15,1.68,1.03,0.36,0.34,0.24,0.12,0,0,0},
    {0,0,0,0,0.31,2.64,1.74,1.64,1.76,1.39,1.24,0.68,0,0,0},
    {0,0,0,0,0,0.25,2.3,1.73,1.86,2.07,1.78,1.52,0,0,0},
    {0,0,0,0,0,0,0.24,1.67,1.57,1.39,1.93,0.88,0.11,0.25,0},
    {0,0,0,0,0,0,0,0.12,1.73,0.69,0.66,1.24,0.22,0,0},
    {0,0,0,0,0,0,0,0,0.1,2.13,0.83,0.84,0.33,0,0},
    {0,0,0,0,0,0,0,0,0,0.05,1.66,0.88,0.11,0.75,0},
    {0,0,0,0,0,0,0,0,0,0,0,1.72,0.78,0.25,0},
    {0,0,0,0,0,0,0,0,0,0,0,0.04,2.11,1.5,0},
    {0,0,0,0,0,0,0,0,0,0,0,0,0.11,2.5,0},
    {0,0,0,0,0,0,0,0,0,0,0,0,0,0,2},
    {0,0,0,0,0,0,0,0,0,0,0,0,0,0,0}
};
```

The elements of the connectivity matrix are defined as the number of branches statistically coming from the upper level branches. For example, CM(i, j) means the number of branches at the level j can be generated from one branch at the level i. Let us use P(i, j) for the probability that a branch at the level i will lead to a branch at the level j. Mathematically it can be expressed in the following equation:

$$P(i, j) = CM(i, j) / SUM\{ CM(i, j), j\}$$

Assume the blood cell starts the trip from the branch 1, it may lead to the branch with the probability of P(1, 1). It may lead to the branch 2 with the probability of P(1, 2). Finally the blood cell will reach the final branch level, i.e. 15. Then the blood cell will pass through the pulmonary sheet. In the same approach, the blood cell will pick a certain route to finish the journey in the venous tree until it complete the circulation. Using the generated probability matrixes, a simulation can be developed to calculate the transit time and blood pressure distributions given certain conditions.

3.2 Transit time calculation

Calculate the exit pressure

The transit calculation includes two steps: exit pressure and transit time. The exit pressure in artery and vein can be generated based on equation 2.2. The computer codes (C++) are shown as the following. For pulmonary sheet, equation 2.6 can be used.

```
double CalculatePressureExit(int Order, double PEntry)
{
    double PExit, tmp1, tmp2;
    int i = Order;

    tmp1 = 640.0*u[i]*B[i]*L[i]/PI/pow(D0[i],4)*Q[i];
    tmp2 = pow((1+B[i]*PEntry),5);

    if (tmp1 >= tmp2-1)
        PExit = PEntry;
    else
        PExit = (pow(-tmp1+tmp2,0.2)-1)/B[i];

    return PExit;
}
```

Calculate the transit time for one section of tube

For a cylindrical elastic tube, the schematic drawing is shown in the following figure.

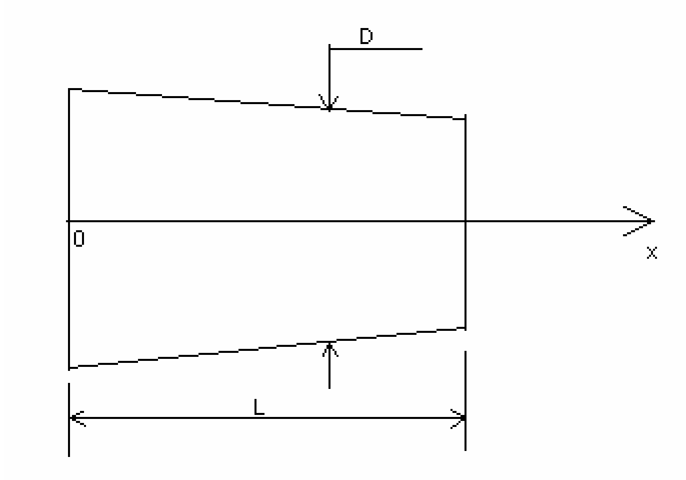


Figure 3.1 Schematic drawing of a vessel tube

The volume of this tube can be derived as:

$$V = \int_0^L \frac{\pi D^2}{4} dx \tag{3.1}$$

Substituting equation $D = D_0 (1 + \beta P)$ in [12] into above equation (3.1), and together with the following boundary conditions:

$$P = P_{entry} \quad \text{for x = 0 and} \quad P = P_{exit} \quad \text{for x = L} \tag{3.2}$$

We can get the following equation:

$$V = \frac{\pi}{4} D_0{}^2 L\left(1 + \beta P_{entry} + \beta P_{exit} + \frac{1}{3}\beta^2 P_{entry}{}^2 + \frac{1}{3}\beta^2 P_{exit}{}^2 + \frac{1}{3}\beta^2 P_{entry} P_{exit}\right) \tag{3.3}$$

The computer codes are shown as the following.

```
double CalculateTransitTime(int Order, double PEntry, double PExit)
{
	double TransitTime, V, tmp;
	int i = Order;

	tmp = 1 + B[i]*(PEntry + PExit) + 1/3.0*B[i]*B[i]*(PEntry*PEntry + PExit*PExit + PEntry*PExit);

	// Volume
	V = PI/4*D0[i]*D0[i]*L[i]*tmp;

	TransitTime = V / Q[i];

	return TransitTime;
}
```

Once a blood cell completes a whole trip in the above described journey, the transit time and pressure values are calculated. The values are called one sample. Hundreds and thousands of calculations can be used to confirm the distribution patterns. Primitive experiments showed that it took less than 1 second to run one sampling even in an inexpensive personal computer (1.0 GHz processor, 640 MB RAM). The later experiments also showed that when the sampling size reached 100, a stabilized distribution pattern could be obtained.

Transit time for capillary sheet

To simplify the analysis, theoretical transit time distributions presented by Fung 4 are applied in this thesis.

Total pulmonary transit time

For example, in a random route, a blood cell travels the branching levels of 15-14-13-12-11-9-6-3-1 for arteries, capillary sheet, and branching levels of 1-3-5-9-11-12-14-15 for veins. All these steps need transit times of 271, 328, 469, 407, 408, 307, 281, 14, 34, 5260, 114, 249, 192, 112, 101, 138, 105, and 118 ms. Thus it took the blood cell a total of 8917 ms to travel through the whole pulmonary system. Appendix I shows a flowchart of the computational methods.

4. Results

The results obtained from the computer programming can be seen in Figures 4.1-4.3. In Figure 4.1 it can bee seen that a peak frequency of 193 examples was obtained around 2300 ms.

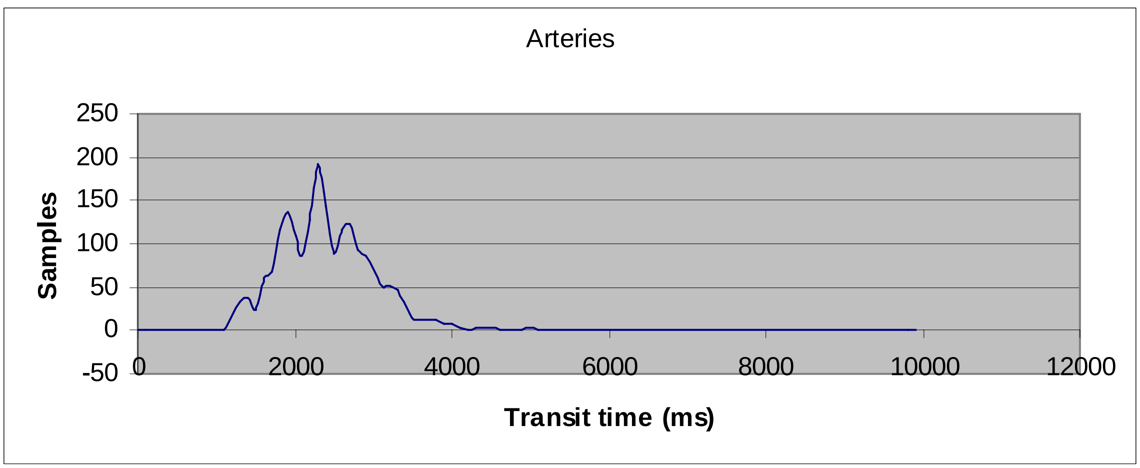


Figure 4.1 Distribution of transit time for arteries

The capillary sheet (Figure 4.2) achieved a peak frequency of 448 2000 ms, and it had a distribution similar to what was calculated by Fung.

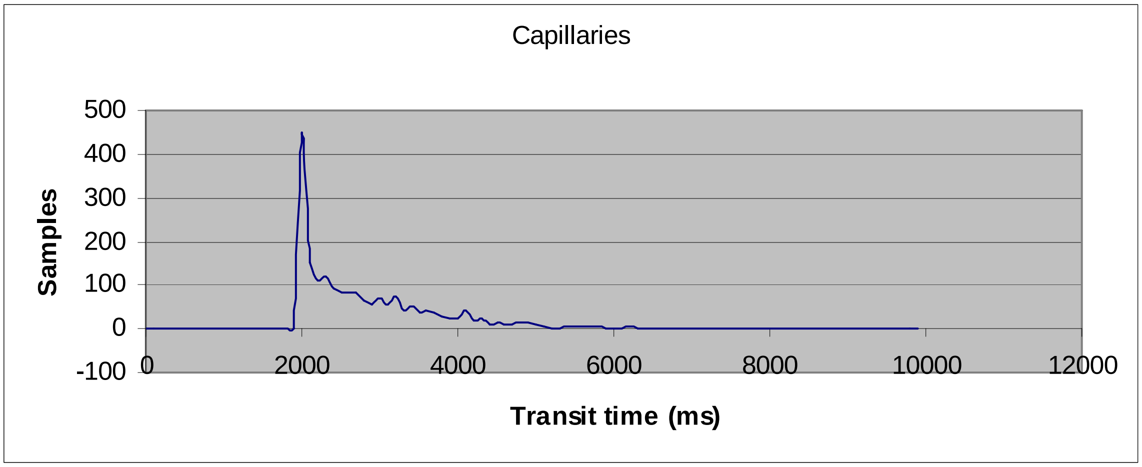


Figure 4.2 Distribution of transit time for capillaries

Then the distribution of the veins can be observed in Figure 4.3. The veins had a peak frequency of 193 2000 ms. The veins had shorter average transit times. The distribution peak also more spread out than in arteries.

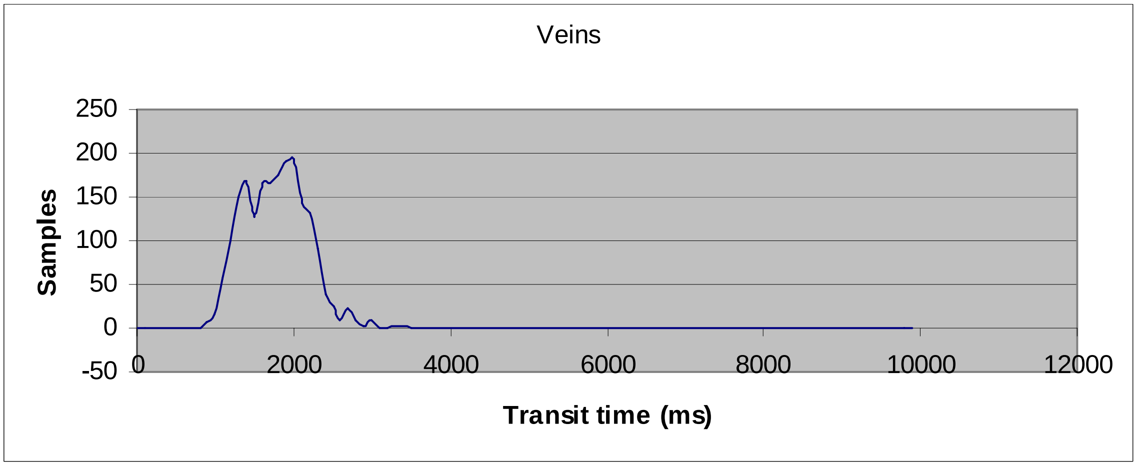


Figure 4.3 Distribution of transit time for veins

Overall the transit time distribution is shown in Figure 4.4. It has the peak frequency of 89 at the transit time of 6700 ms.

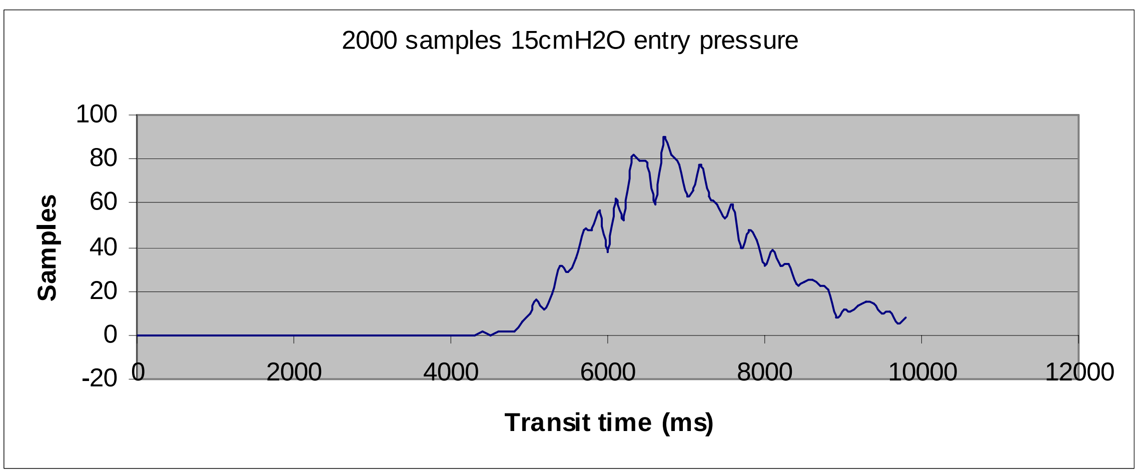


Figure 4.4 Distribution of transit time

5. Discussion

One assumption of the model is steady blood flow in the pulmonary circulation. All parameters used in the modeling remain constant while the pressure and flow change. The literature supports these assumptions, which hold true in a low pressure system like the pulmonary circulation.

Another assumption is the same order of the vessels share the same length, which means a linear branching system. In reality the vessel lengths are different. However, in the equation of the pressure-flow rate for the pulmonary system, the length is the first power while the diameter is the fifth power. The diameter is much more significant than the length. This issue is taken care of in the Diameter-Defined Strahler System which is applied in this thesis.

In the current modeling method, there is no resistance at the branching intersections. Since there is little energy lost at the intersections in such a low pressure biological system, we can assume there is no pressure and flow change at the branching points.

This stochastic simulation converges quickly. The defined curve for the transit time distribution for the whole pulmonary circulation is achieved when the sample size reaches 200. The following figure shows how the distribution curves change when we increase the sample sizes from 1000 to 10000. The transit times for the peak frequency remain the same for different sample sizes.

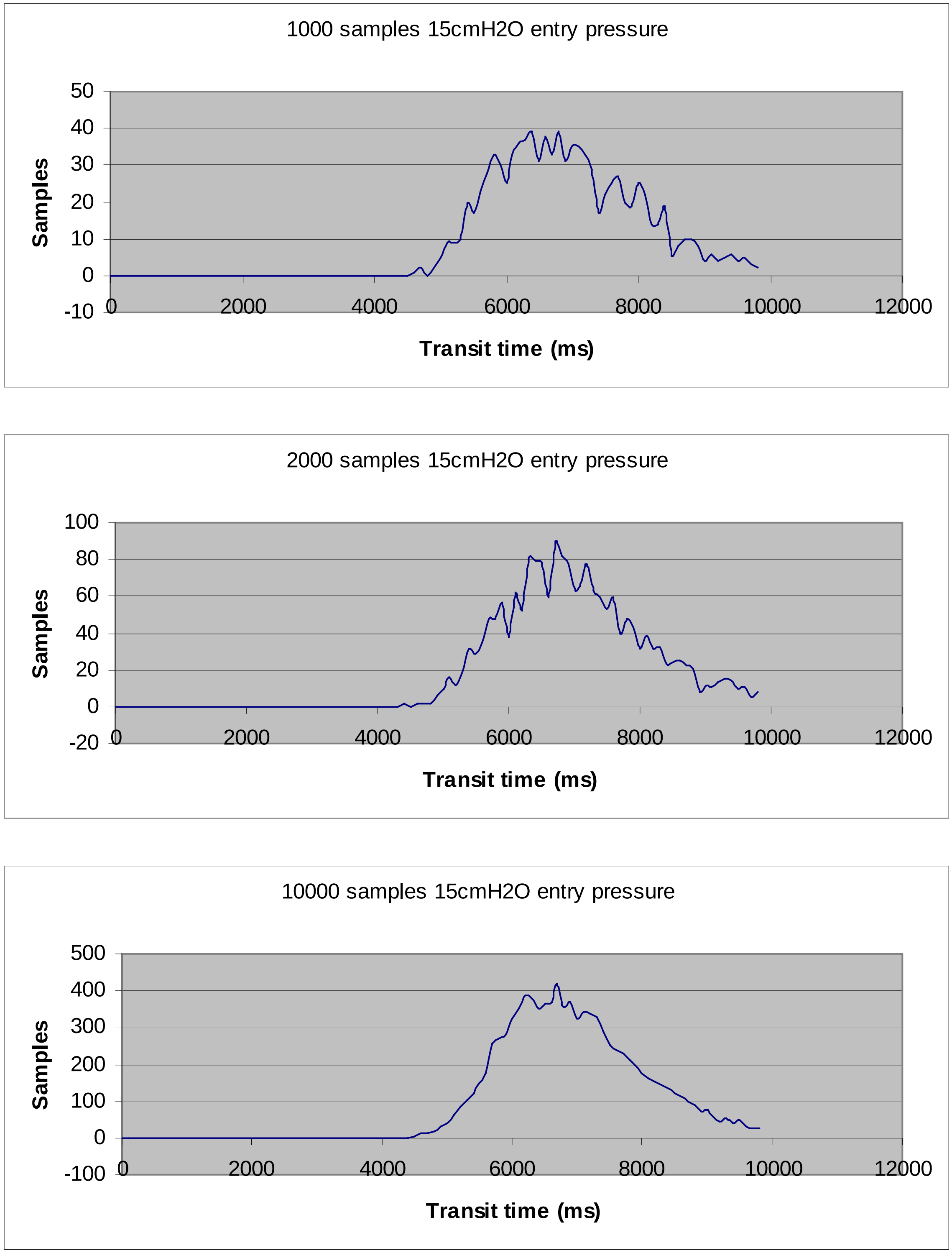
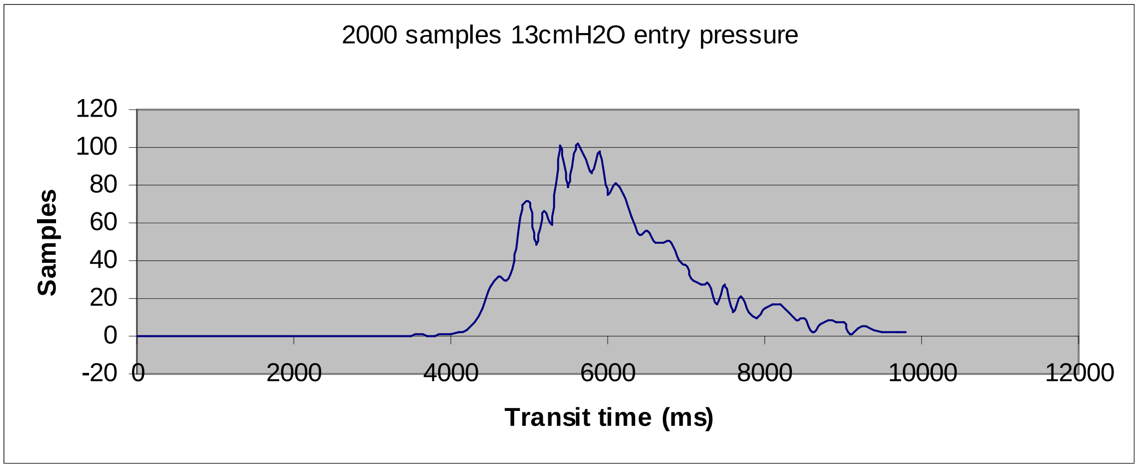
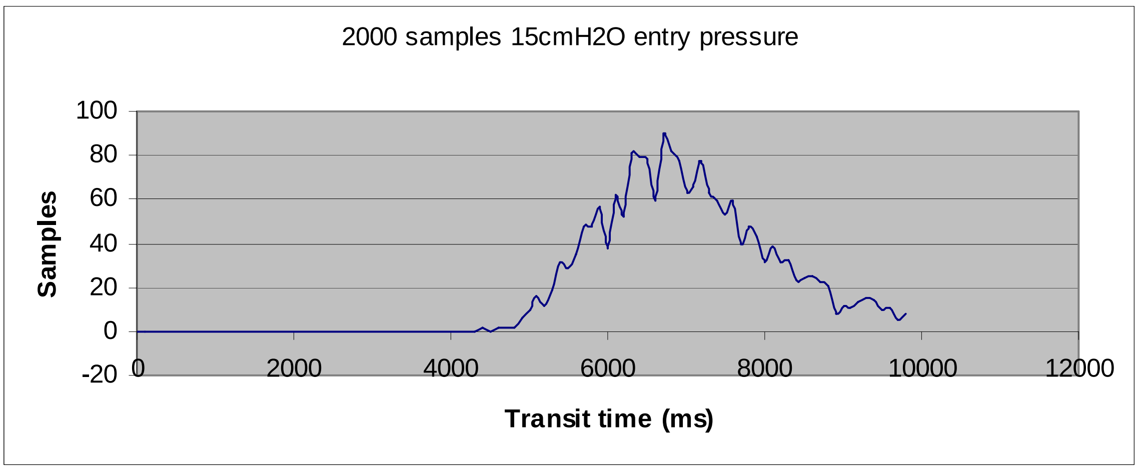


Figure 5.1 Transit times with different sample sizes

The entry pressure is one of the key parameters which reflects the lung condition and are worth investigation. The results with different entry pressures are interesting. The following figure shows the transit time distributions with different entry pressure entering the artery, ranging from 13 cmH2O to 17 cmH2O. When the entry pressure increases, based on the equation (2.2), the exit pressure will increase. Since the pressure is on the fifth order, the pressure dropping across the vessel will decrease. The flow rate will decrease accordingly. It takes more time for the blood cells pass through the pulmonary circulation.





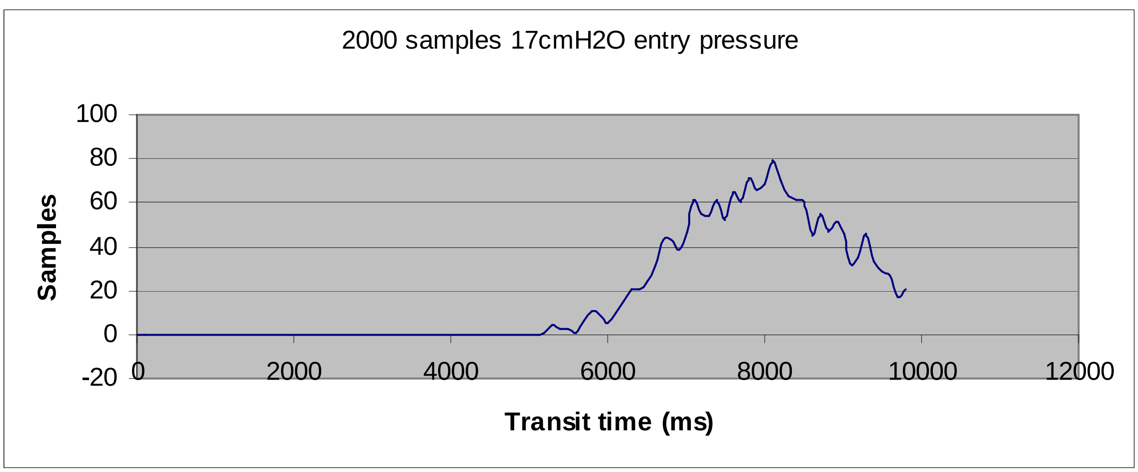
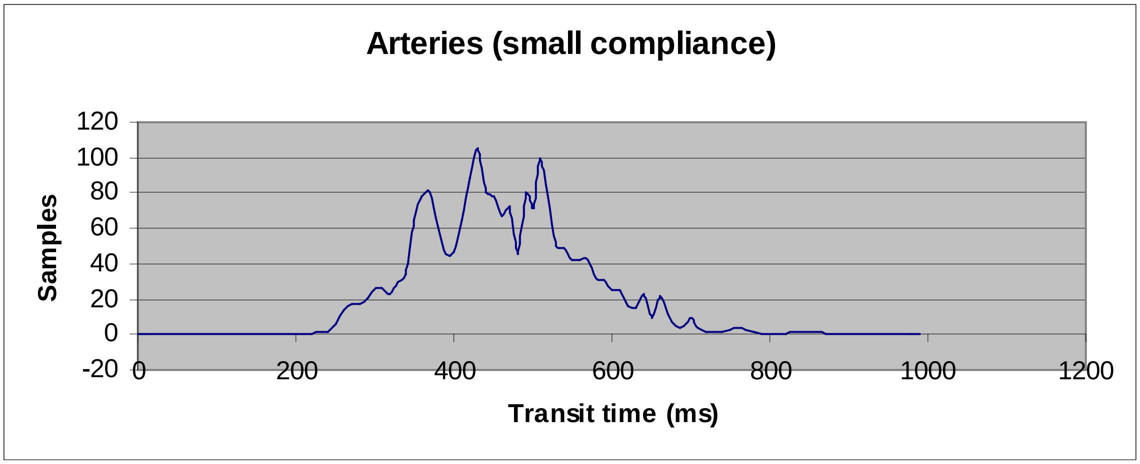


Figure 5.2 Transit times with different entry pressures



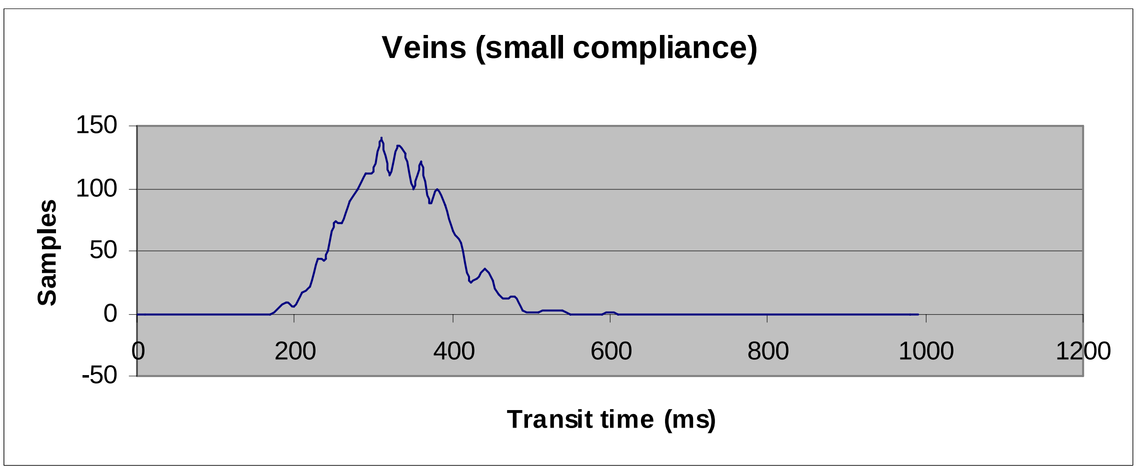


Figure 5.3 Transit time with small compliance conditions

In 1994, Wiggs [16] presented the dissertation work in modeling neutrophil transit through the human pulmonary circulation, in which the pulmonary circulation was considered to be rigid for the modeling. The above figure shows the results if we assign small values of compliances (less than 0.3). The distribution curves share the same pattern of the results from Wiggs' research. However, his dissertation reported the median value was 0.7 seconds for the distribution of arterial transit times and 0.8 seconds for venous transit times, which are higher than the results achieved in this thesis. The main reason is that we are using different types of branching systems. Wiggs used a modified Horsfield branching structure while we applied a Diameter-Defined Strahler System.

6. Conclusion

A new stochastic simulation approach was introduced in this thesis for the whole pulmonary circulation of the human lung. No similar models were found in the literature at the time of writing. First, the connectivity data between different levels of the pulmonary system is converted into a probability matrix. Second, the stochastic simulation model simulates the blood flow in the hierarchical structure of a pulmonary circulation system without constructing the whole structure. At the same time, the model calculates the transit time and outputs the blood pressure. Third, the model is able to efficiently produce the transit time frequency distribution of the human arterial and venous trees. Final, the transit time distributions of the whole pulmonary circulation are collected. Such a simulation model has the advantage of the low computing cost and the high flexibility.

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APPENDIX I: ALGORITHM USED IN THE COMPUTATIONAL MODEL OF HUMAN PULMONARY BLOOD CIRCULATION